

# Bioidentical hormone micronized progesterone

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## Clinical question

Is “bioidentical” micronized progesterone (MP) instead of “synthetic” medroxyprogesterone acetate (MPA) safer and better for menopausal symptom control?

## Evidence

Here is some of the evidence comparing MP with MPA.

- Menopausal symptoms and tolerability
  - An RCT (N=875): no difference in symptoms<sup>1</sup> or in bleeding episodes<sup>2</sup> (when both used cyclically).
  - Survey study<sup>3</sup> (N=176): improvement in quality of life, but patients had already switched from MPA to MP, potentially biasing the results.
- Cardiovascular disease
  - An RCT<sup>4</sup> (N=875, 3 years): MP had slightly greater effect on high-density lipoprotein levels (increase of <0.1 mmol/L), but clinical outcomes not recorded.
- Venous thromboembolism
  - Case-control study<sup>5</sup>: neither MP nor MPA had an effect.
- Breast cancer
  - Cohort study<sup>6,7</sup> (99 000 postmenopausal women): authors suggest MP might be preferred to most synthetic progestins; validity in question (imbalance in estrogen treatment; multiple subgroup analyses, some apparently post hoc; and selective grouping of high-risk progestins).
- A number of other studies are too small (<25 patients) to provide any meaningful information.<sup>8-10</sup>

## Context

- Reliance on observational studies, small RCTs, and surrogate end points is reminiscent of when synthetic hormones were believed to reduce coronary artery disease by 35% to 50%.<sup>11,12</sup> Later, a large well-designed RCT showed increased cardiovascular events.<sup>13</sup>
- The Endocrine Society warns claims of improved safety or effectiveness are unproven.<sup>14</sup> The Society of Obstetricians and Gynaecologists of Canada and others<sup>15</sup> strongly recommend against compounding of bioidentical hormones.

## Bottom line

The theoretical advantages of MP are not supported by the evidence. We risk repeating errors of the past by concluding MP is more or less safe or efficacious than other hormone replacement therapy (HRT) without results of large RCTs. Compounding of bioidentical hormones only serves to “compound” the uncertainty.

## Implementation

The Women’s Health Initiative<sup>13</sup> found combined HRT increased breast cancer, venous thromboembolism,

myocardial infarction, and stroke by 8, 18, 7, and 8 events in 10 000 patient-years, respectively; HRT decreased colorectal cancer and hip fracture by 6 and 5 less events in 10 000 patient-years, respectively. However, HRT is the most effective therapy for menopausal symptoms, particularly hot flashes.<sup>16</sup> Patients desiring treatment should be advised that there is no convincing evidence that bioidentical hormones are safer or more effective than synthetic HRT. Overall, if 100 women take synthetic HRT for 5 years, there will be 1 more serious adverse event relative to benefit.<sup>13</sup>

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The opinions expressed in this Tools for Practice article are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

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